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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/499,006	02/04/2000	Dr. Paddy Jim Baggot	249/127	9604

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EXAMINER	
JOHANNSEN, DIANA B	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 09/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/499,006	BAGGOT, DR. PADDY JIM	
	Examiner	Art Unit	
	Diana B. Johannsen	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 15-24* is/are pending in the application.

4a) Of the above claim(s) *1 and 17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-16 and 18-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 25, 2005 has been entered. Claims 15 and 21 have been amended, and claims 15-16 and 18-24 are under consideration. Claims 1 and 17 remain withdrawn from consideration (see below).

Election/Restriction

2. Claims 1 and 17 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 13.

Claim Rejections - 35 USC § 112, first paragraph

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 15-16 and 18-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of identifying Down Syndrome in a fetus in which decreased levels of formiminoglutamic acid in amniotic fluid (as compared to a normal control) and/or increased levels of oxalic acid in amniotic

fluid (as compared to a normal control) are detected, does not reasonably provide enablement for methods in which abnormal levels of any metabolite or combination of metabolites identified in amniotic fluid is considered to be indicative of Down Syndrome. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: (A) the breadth of the claims; (B) the nature of the invention; (C) the state of the prior art; (D) the level of one of ordinary skill; (E) the level of predictability in the art; (F) the amount of direction provided by the inventor; (G) the existence of working examples; and (H) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) (*MPEP* 2164.01(a)).

The claims are drawn to methods of identifying Down Syndrome in a fetus in which abnormal quantities of a metabolite or combination of metabolites in an amniotic fluid sample is considered to be an indicator of the presence of Down Syndrome. With regard to claim 16, it is noted that the claim merely requires that the control profile of the claims (which already includes "each metabolite in amniotic fluid" – see step d) of claim 15) include the recited metabolites; the claim does not require that any of the recited metabolites be present at an abnormal level in the specimen of the claims. Similarly,

with regard to claim 24, the claim merely requires that the quantities of 2 particular metabolites be identified; the claim does not indicate that one or both of these metabolites must be present in an "abnormal quantity" in the tested specimen. With regard to claims 22-23, the claims encompass decreased formiminoglutamic acid and increased oxalic acid, but also include several "abnormal quantities" not supported by the data in the specification (see below).

It is unpredictable as to whether one of skill in the art could use applicant's invention in a manner reasonably commensurate with the claims. The specification discloses that the mean and median levels of several metabolites in a population of "Down Syndrome patients" differ from the mean and median levels found in a population of "normal patients" (see data presented at pp. 7-16). However, of the differences in metabolic levels reported by applicant, only a very few appear to be statistically significant. With regard to the particular metabolites of applicant's dependent claims, applicant shows that the median level of formiminoglutamic acid present in amniotic fluid differs significantly in normal as compared to Down Syndrome patients (p-value of 0.007; see Table 10), as does the median value of oxalic acid (p-value of 0.007; see Table 12). However, the mean and median levels of serine and homocysteine (see Tables 5 and 6), and normetanephrine (Tables 7 and 8) do not appear significantly different in a normal population as compared to a Down Syndrome population, and levels of tetra-hydro-biopterin are not reported for either population. Further, applicant's data shows that the vast majority of metabolites present in amniotic fluid are not present at statistically different levels in a Down Syndrome population as compared to a normal

population (see pages 7-16). Thus, while the specification provides evidence of two metabolites whose levels would reasonably be considered by one of skill in the art when diagnosing Down Syndrome, these two metabolites are clearly not representative of amniotic fluid metabolites as a whole, and the teachings of the specification do not support enablement of the invention as broadly claimed. Absent guidance from the specification, one of skill in the art may rely on the teachings of the prior art for enablement of a claimed invention. However, in the instant case, the prior art is silent with respect to methods in which differences in the quantities of a plurality of metabolites in amniotic fluid are employed in the diagnosis of Down Syndrome. Thus, neither the specification nor the art provide evidence that one may diagnose Down Syndrome in a fetus by comparing levels of amniotic fluid metabolites other than formiminoglutamic acid and oxalic acid. As the vast majority of metabolites present in amniotic fluid do not appear to differ significant in Down Syndrome patients as compared to normal patients, it would require undue experimentation to practice applicant's invention in a manner commensurate in scope with the claims.

Claim Rejections - 35 USC § 112, second paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 22-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 22-23 are indefinite over the recitation of the limitation "the identifying step" in each of the claims. Claim 21, from which claims 22-23 depend, recites 3 different steps of "identifying," and it is not clear which of these would be considered to constitute "the identifying step" of the dependent claims.

Claim 22 is further indefinite because the claim as written does not make clear with respect to what the various recited metabolites are "increased" or "decreased." Clarification is required.

Conclusion

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Diana B. Johannsen whose telephone number is 571/272-0744. The examiner can normally be reached on Monday-Friday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones can be reached at 571/272-0745. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Diana B. Johannsen
Primary Examiner
Art Unit 1634
September 28, 2005